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10/069,767	02/22/2002	Douglas J. DeMarini	P50996	3807

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EXAMINER

WILDER, CYNTHIA B

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/069,767

Applicant(s)

DEMARINI ET AL.

Examiner

Cynthia B. Wilder, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 2/22/2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 02-22-2002.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

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DETAILED ACTION

1. Applicant's preliminary amendment filed on 2/22/2002 is acknowledged. However, the amendment to the abstract was not entered because the clean copy of the amendment and marked-up version with marking to show changes made are not the same. Specifically, the version with marking shows a fragmented sentence ending with "comprising" whereas, the clean copy of the amendment ends with "recombination". Appropriate correction is required.

Information Disclosure Statement

2. The information disclosure statement filed on 2/22/2002 is acknowledged and has been entered.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1-19 are confusing in claims 1, 3, 17 and 19 for the recitation of the phrase "inserting into a recombination-competent cell the following first nucleic acids" because it appears that additional nucleic acids *not* a part of the first nucleic acids are encompassed in the claimed methods. However, no "subsequent" or "second nucleic acids" are recited. Likewise, a nexus between "the final generating step" and the "inserting step" comprising "the first nucleic acids" is unclear. Clarification is required.

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(b) Claims 1-19 are confusing in claims 1, 3, 14, 15, 17 and 19 at step (iii) for the recitation of "a combined length of no more than 45 nucleotides" or "a combined length of no more than 40 nucleotides" because it implies that the linker comprises more than one element. However, it cannot be determine what "combined elements" are encompassed by the linker. Further, it cannot be determined if Applicant is making reference to steps (i) and (ii) as being the "combined" elements of the linker or if reference is being made to a separate entity. Clarification is required as to Applicant intent.

(c) Claim 3 is indefinite in line 1 for the recitation of "into of claim 1" because it unclear as to what the "insert polynucleotide" is being inserted into. Appropriate correction is required.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zervos et al (WO 99/40208, 12 August 1999) and Raymond et al (Biotechniques, Vol. 26: 134-141, 1999) and further in view of Sung et al (CA 1 3030 527 A).

Regarding claim 1, 3, 6-15, 17 and 19, Zervos et al teach a method of inserting, cloning or subcloning an insert polynucleotide into a target nucleic acid having a first end and a second by homologous recombination comprising inserting into a recombination-competent cell, one or more insert polynucleotides comprising an insert segment and at least one linker comprising a combined length of at least 20 30, 40, 50, 60 or more base pairs in length and generating with the cell a nucleic acid or vector containing the insert segments inserted between the first and second ends in an order defined by recombination sequences found in the target nucleic acid and insert polynucleotides (page 2, lines 1-37 to page 3, lines 1-2; page 6, lines 10-11 and page 19, lines 17-34). Zervos et al differs from the instant invention in that the reference does not teach wherein the linker sequence is a substantially single-stranded recombination sequence, a recombination sequence of no more than 25 base pairs or a combined length of no more than 45 or 40 nucleotides in length. In a method similar to that of Zervos et al, Raymond et al teach a method of inserting, cloning or subcloning an insert polynucleotide into a target nucleic acid sequence having a first end and a second end by homologous recombination comprising the steps of inserting into a recombinant-competent cell one or more polynucleotide having an insert segment and at least one linker comprising a recombinant sequence, wherein the combined length is at least about 60 base pairs and generating in the cell a nucleic acid containing the insert segment in an order defined by recombination (see results section and Figures 1-5). Raymond et al further teach that shorter, synthetic linkers could be used to recombine donor and acceptor

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sequences (page 138, col. 2, first paragraph). Zervos et al and Raymond et al differ from the instant invention in that the reference does not teach wherein the linker sequence is a substantially single-stranded recombination sequence or a recombination sequence of no more than 25 base pairs or a combined length of no more than 40-45 nucleotides in length.

Sung et al teach "cross-over linkers" for use in methods of inserting new sequences, deleting old sequences or modifying sequences or a combination of the filling in cloning vehicles, especially plasmids (page 1, first paragraph). Sung et al teach wherein the linkers may be substantially single stranded or double stranded (page 4, lines 25-26) and wherein said linkers comprises a combined length of no more than 40-45 nucleotides in length (page 14, linkers p-12, p-13, p-4a, p-5a and p-4). Sung et al teach that linkers comprising short sequences are effective in methods of homologous recombination and when in single stranded form appears to be advantageous in avoiding the generation of mutant plasmid associated with the usage of duplex linkers (page 4, lines 17-23; bottom of page 26 to page 27, lines 1-5, 9-10 and page 37, 1-7). Therefore, in view of the foregoing, one of ordinary skill in the art would have been motivated to have modified the homologous recombination method of Zervos et al and Raymond et al to have encompass insert polynucleotides comprising a linker sequence that is substantially single stranded and no longer than 45 nucleotides in length based on the teaching of Sung et al that linkers comprising short sequences are effective in methods of homologous recombination and when in single stranded form appears to be advantageous in avoiding the generation of mutant plasmid associated with the usage of duplex linkers.

Regarding claim 2, Zervos et al teach the embodiment of claim 1, comprising inserting an insert polynucleotide into genomic nucleic acid (bottom of page 3 to top of page 4, lines 1-4).

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Regarding claim 4, Raymond et al teach the embodiment of claim 1, comprising inserting a single insert polynucleotide derived insert segment into the vector (abstract).

Regarding claim 5, Zervos et al teach the embodiment of claim 1 comprising inserting a multiple polynucleotide-derived insert segment in a defined orientation dictated by recombination sequences (page 2, lines 1-37 to page 3, lines 1-2).

Regarding claim 16, Zervos et al teach wherein the vector generated is animal gene replacement targeting vector comprising an animal specific selectable marker and a selectable marker specific for the recombination-competent cell (page 15 and 16, section entitled "vector and host cell").

Regarding claim 18, Sung et al teach the embodiment of claim 17, wherein the linker nucleic acids are synthesized without the use of an enzyme-catalyzed amplification reaction (page 12, example 1).

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Cynthia Wilder
CYNTHIA WILDER
PATENT EXAMINER
10/18/2004